

CLAIMS

1. A method for selecting an immunosuppressive agent with a less thrombocytopenia effect, said method comprising the following items (1) and (2):

(1) selecting compounds having an immunosuppressive activity; and

(2) selecting a compound having a weak GATA-1 transcription inhibitory activity from the compounds selected in (1).

2. A method for selecting an immunosuppressive agent with a less thrombocytopenia effect, said method comprising the following items (1) to (3):

(1) measuring an immunosuppressive activity of an analyte;

(2) measuring a GATA-1 transcription inhibitory activity of the analyte; and

(3) comparing the immunosuppressive activity determined in (1) with the GATA-1 transcription inhibitory activity determined in (2) to select an immunosuppressive agent with a less thrombocytopenia effect.

3. A method for selecting an immunosuppressive agent with a less thrombocytopenia effect, said method comprising the following items (1) to (3):

(1) measuring an IL-2 transcription inhibitory activity in a test cell in the coexistence of the test cell and an analyte;

(2) measuring an GATA-1 transcription inhibitory activity in a test cell in the coexistence of the test cell and an analyte; and

(3) comparing the IL-2 transcription inhibitory activity determined in (1) with the GATA-1 transcription inhibitory activity determined in (2) to select an immunosuppressive agent with a less thrombocytopenia effect.

4. A method for selecting an immunosuppressive agent with a less thrombocytopenia effect, said method comprising the following items (1) to (3):

(1) measuring an IL-2 transcription inhibitory activity in a test cell into which an IL-2 reporter gene has been introduced in the coexistence of the test cell and an analyte;

(2) measuring a GATA-1 transcription inhibitory activity in a test cell into which a GATA-1 reporter gene has been introduced in the coexistence of the test cell and an analyte; and

(3) comparing the IL-2 transcription inhibitory activity determined in (1) with the GATA-1 transcription inhibitory activity determined in (2) to select an immunosuppressive agent with a less thrombocytopenia effect.

5. A method for selecting an immunosuppressive agent with a less thrombocytopenia effect as claimed in Claim 4, comprising measuring a (IL-2 IC50) value as an IL-2 transcription inhibitory activity, measuring a (GATA-1 IC50) value as a GATA-1

transcription inhibitory activity, and comparing both the values.

6. A method for selecting an immunosuppressive agent with a less thrombocytopenia effect as claimed in Claim 5, comprising selecting a compound having the $(\text{GATA-1 IC}_{50}) / (\text{IL-2 IC}_{50})$ value of 5 or more.

7. A method as claimed in any of Claims 4 to 6, wherein the GATA-1 reporter gene comprises the transcriptional control region of human GATA-1 gene and a reporter gene.

8. A method as claimed in any of Claims 4 to 7, wherein the GATA-1 reporter gene comprises a sequence of the region from -3769 to -3133 upstream of the transcription initiation point and sequence of the region from -789 to +30 proximal to the transcription initiation point of human GATA-1 gene.

9. A method as claimed in any of Claims 4 to 8, wherein the IL-2 reporter gene comprises the transcriptional control region of IL-2 gene and a reporter gene.

10. A method as claimed in any of Claims 4 to 9, wherein the IL-2 reporter gene comprises a sequence of the region from -378 to +54 proximal to the transcription initiation point of human IL-2 gene.

11. A method as claimed in any of Claims 4 to 10, wherein the test cell into which a GATA-1 reporter gene is introduced is a human megakaryocytic cell strain.

12. A method as claimed in any of Claims 4 to 11, wherein

the test cell into which an IL-2 reporter gene is introduced is a human T cell-derived cell strain stimulated by phorbol 12-myristate 13-acetate, ionomycin and anti-CD28 antibody, and the test cell into which a GATA-1 reporter gene is introduced is a human megakaryocytic cell strain.

13. A method as claimed in Claim 12, wherein the human T cell-derived cell strain is a Jurkat cell.

14. A method as claimed in Claim 11, wherein the human megakaryocytic cell strain is a HEL cell.

15. A method as claimed in Claim 12, wherein the human megakaryocytic cell strain is a HEL cell.

16. A method as claimed in any of Claims 4 to 15, wherein the reporter gene is a firefly luciferase gene.

17. A method for selection as claimed in any of Claims 1 to 16, wherein the analyte is an HDAC inhibitor.

18. A method for selecting an immunosuppressive agent with a less thrombocytopenia effect, comprising measuring the amount of expression of GATA-1 protein.

19. A method for selecting an immunosuppressive agent with a less thrombocytopenia effect, said method comprising the following items (1) to (3):

(1) measuring the amount of expression of IL-2 protein;

(2) measuring the amount of expression of GATA-1 protein;

and

(3) comparing both the amounts of expression to select

an immunosuppressive agent with a less thrombocytopenia effect.

20. A kit for measurement in selecting an immunosuppressive agent with a less thrombocytopenia effect, comprising the following items (1) and (2):

(1) a DNA construct containing a GATA-1 reporter gene;
and

(2) a test cell of megakaryocytic cell line.

21. A kit for measurement in selecting an immunosuppressive agent with a less thrombocytopenia effect, comprising the following items (1) to (4):

(1) a DNA construct containing an IL-2 reporter gene;

(2) a DNA construct containing a GATA-1 reporter gene;

(3) a test cell of T-cell line; and

(4) a test cell of megakaryocytic cell line.

22. An HDAC inhibitor with a less thrombocytopenia effect, said inhibitor being selected by a method as claimed in Claim 17.

23. An immunosuppressive agent with a less thrombocytopenia effect, said agent being selected by a method for selection as claimed in any of Claims 1 to 16.

24. An immunosuppressive agent for treatment of inflammatory disorders, diabetes mellitus, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukemia, protozoal infections, organ transplant rejection, autoimmune diseases, and tumors, said

agent comprising as an active ingredient an HDAC inhibitor as claimed in Claim 22.

25. A therapeutic agent for treatment of inflammatory disorders, diabetes mellitus, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukemia, protozoal infections, organ transplant rejection, autoimmune diseases, and tumors, said agent comprising as an active ingredient an immunosuppressive agent as claimed in Claim 23.

26. A therapeutic method for treatment of inflammatory disorders, diabetes mellitus, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukemia, protozoal infections, organ transplant rejection, autoimmune diseases, and tumors, said method comprising administering an immunosuppressive agent with a less thrombocytopenia effect containing as an active ingredient an HDAC inhibitor as claimed in Claim 22.

27. A therapeutic method for treatment of inflammatory disorders, diabetes mellitus, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukemia, protozoal infections, organ transplant rejection, autoimmune diseases, and tumors, said method comprising administering an immunosuppressive agent with a less thrombocytopenia effect containing as an active ingredient an immunosuppressive agent as claimed in Claim 23.

28. Use of an HDAC inhibitor as claimed in Claim 22 in manufacture of a therapeutic agent for treatment of inflammatory disorders, diabetes mellitus, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukemia, protozoal infections, organ transplant rejection, autoimmune diseases, and tumors.

29. Use of an immunosuppressive agent as claimed in Claim 23 in manufacture of a therapeutic agent for treatment of inflammatory disorders, diabetes mellitus, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukemia, protozoal infections, organ transplant rejection, autoimmune diseases, and tumors.